Cyclic Acetylenes. V. Syntheses and Properties of Strained Cyclic Ethers of o, o′-Dihydroxydiphenyldiacetylene

By Fumio TODA and Masazumi NAKAGAWA

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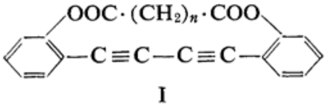
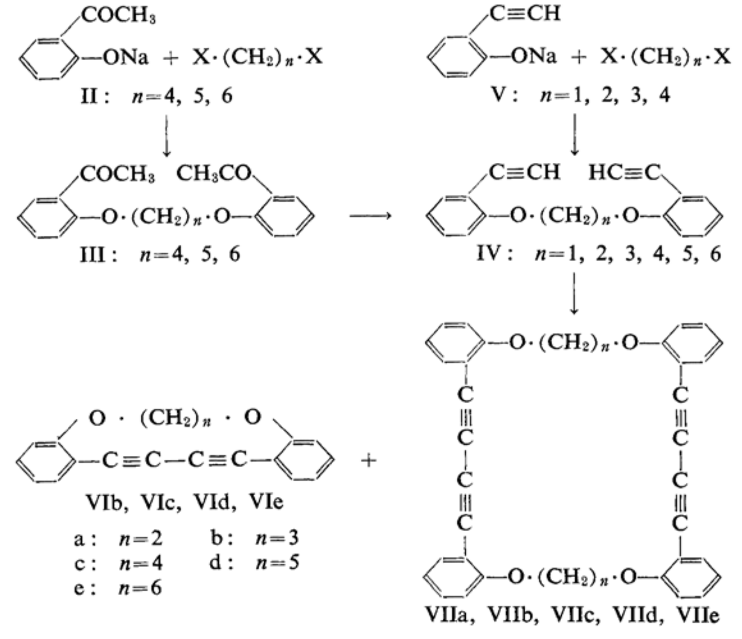
In the previous paper of this series¹⁾, the present authors reported the syntheses and the ultraviolet spectroscopic properties of a series of diacetylenic macrolides (I, n=3, 4, 5 and 7). In the course of the synthesis of the compound I, it was found that the ester linkages are cleft when the number of methylene groups is 2 or 3 yielding 2,2′-dibenzofuranyl and other related compound, and the cleavage of the ester linkage was attributed to the large ring strain involved in I. The present paper deals with the syntheses of a series of analogous cyclic diacetylenes in which the ester linkage is replaced by the ether linkage to avoid the cleavage reaction in the course of the ring closure. The synthesis was carried out according to the following series of reactions.


I

The diketone III which was obtained by the reaction of polymethylene dihalide (n=4, 5 and 6) with sodium salt of o-hydroxyacetophenone (II) was treated with phosphorus pentachloride to yield the chloro-derivative. The chloro-derivative was dehydrochlorinated with sodamide in liquid ammonia to yield the terminal diacetylene IV, (n=4, 5 and 6).

The terminal diacetylene IV, (n=1, 2, 3 and 4) was also prepared by the reaction of sodium o-ethynylphenoxide (V) with polymethylene dihalide (n=1, 2, 3 and 4). The terminal diacetylene IV thus obtained was submitted to the oxidative coupling reaction according to Eglinton's procedure²⁾. The yields of the cyclic diacetylenes VI_b, VI_c, VI_d and VI_e formed by the intramolecular oxidative coupling were found to be 3, 40, 40 and 40%, respectively. In the case of n=2, the cyclic diacetylene could not be isolated from the reaction mixture. This is probably attributable to the high strain which may arise from the ring formation. The cyclic tetraacetylenes VII_a, VII_b, VII_c and VII_e which are the products of the bimolecular


II: n=4, 5, 6

V: n=1, 2, 3, 4

III: n=4, 5, 6

IV: n=1, 2, 3, 4, 5, 6

VIb, VIc, VId, VIe

a: n=2 b: n=3

c: n=4 d: n=5

e: n=6

VIIa, VIIb, VIIc, VIId, VIIe

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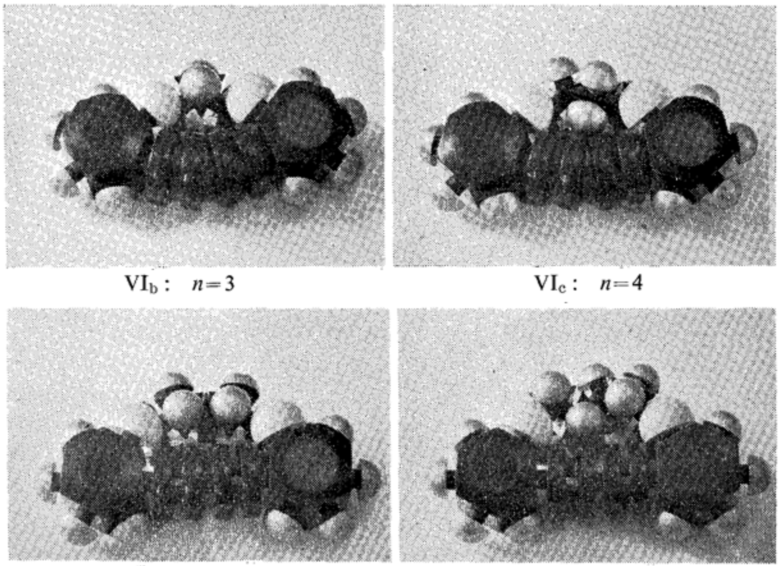
1) F. Toda and M. Nakagawa, This Bulletin, **33**, 223 (1960).

2) G. Eglinton and A. R. Galbraith, *Chem. & Ind.*, **1956**, 737; *J. Chem. Soc.*, **1959**, 889.



VI_b: $n=3$ VI_c: $n=4$

VI_d: $n=5$ VI_e: $n=6$

Fig. 1. The molecular models of VI (Courtauld model).

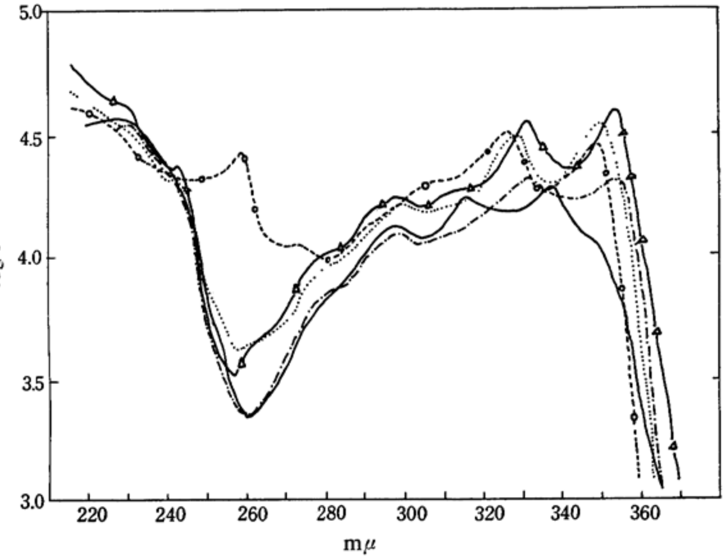


Fig. 2. The ultraviolet spectra of the cyclic diacetylenes (VI) and $VIII_a$.

———— : VI_b in 99.5% ethanol

—·—· : VI_c in 95% ethanol

—△—△ : VI_d in 95% ethanol

········ : VI_e in 95% ethanol

--○--○ : $VIII_a$ in 95% ethanol

coupling reaction were isolated from the reaction mixture in the yield of 2.5, 1, 2, trace and 10%, respectively. The formation of a cyclic dimer is an interesting contrast to the fact that the oxidative coupling of di-*o*-ethynylphenyl polymethylene dioate gave only the monomeric cycle I and the formation of the dimeric tetraacetylene was not observed[1].

The structures of VI and VII were determined by the analytical data, molecular weight determination and ultraviolet and infrared spectroscopic evidences. VI is a fairly stable compound, except in the case of VI_b which is found to be unstable to heat. The molecular weight of VI_b could not be determined by the Rast method due to its thermal instability; therefore the molecular weight was estimated by the X-ray method*.

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* The determination of molecular weight by the X-ray method was kindly performed by Dr. Y. Tomiie of the Laboratory of Physical Chemistry of this Department to whom the authors express their sincere gratitude.

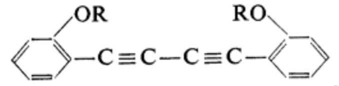
TABLE I

Compound	Solvent	Absorption					
VI$_b$	E	231 (300)	298 (111)	316 (144)	337 (159)		
VI$_c$	E*	230 (345)	299 (122)	331 (201)	353 (199)		
VI$_d$	E*	243 (218)	299 (161)	331 (317)	353 (365)		
VI$_e$	E*	242 (203)	299 (158)	328.5 (297)	349 (336)		
VII$_a$	D	260 (285)	**272** (112)	310 (186)	324 (240)		344 (174)
VII$_b$	D	259.5 (100)	**276** (76)	310 (135)	324 (232)		351 (216)
VII$_c$	D	261 (350)	**275** (105)	310 (185)	321 (196)		349 (115)
VII$_d$	D	260 (148)	276 (97)	313 (197)	331 (324)		353 (331)
VII$_e$	D	261 (269)	274 (100)	313 (188)	329 (257)		351.5 (212)
VIII$_a$	E*	259.5 (265)	274.5 (111)	**309** (203)	326 (321)		349 (286)
VIII$_a$	E	259 (260)	273 (107)	**310** (199)	326 (327)		348 (293)
VIII$_b$	E	259.5 (282)	274 (108)	**310** (194)	326 (297)		349 (253)
IX$_a$	D		**280** (91)	299 (199)	320 (333)		343 (390)
IX$_a$	E	**230** (377)	**280** (98)	298 (205)	319 (338)		341 (392)
IX$_b$	E	**230** (395)	**280** (100)	298 (182)	322.5 (241)		341 (248)
XII	E	**230** (399)	**280** (93)	298 (172)	319 (226)		341 (247)
XIII	D	261 (222)	**275** (104)	309 (184)	328 (251)		350 (202)
XV	D	261 (287)	**275** (130)	310 (212)	328 (323)		351 (285)
XV	E	260 (289)	273 (110)	310 (215)	326 (346)		348 (300)
XVII	E	232 (288)	**278** (75)	296 (168)	317 (269)		338.5 (291)
XVIII	E	258 (204)	273 (76)	307 (168)	323.5 (278)		346 (239)
XIX	E*	260 (213)	275 (85)	305 (168)	323 (270)		345 (236)
DDD	E	258 (262)	273 (100)	291 (127)	326 (300)		348.5 (277)
DDD	NaOH aq.	218 (616)	**261** (228)	278 (97)	296 (99)	317 (110)	359 (226)

The figures indicate the λ_{max} in mμ.
The figures in parentheses are $\varepsilon_{max} \times 10^{-2}$.
The bold figures indicate shoulders.
E, E* and D denote 99.5% ethanol, 95% ethanol and dioxane, respectively.
DDD means *o, o'*-dihydroxydiphenyldiacetylene.

It is to be noted that VI$_c$ and VII$_e$ exist in dimorphic forms and the melting points of the former substance were found to be 96 and 112°C, and those of the latter were 184~185°C (stable form) and 207~208°C. The analytical data and the measurement of solvent of crystallization revealed that VII$_b$ contains 2 mol. of benzene.

An examination of the scale model of VI reveals that the polymethylene bridge in VI$_d$ is slightly short and that of VI$_e$ is slightly long to hold the molecule in a uniplanar, strain free conformation, but the ring strain involved in VI$_d$ and VI$_e$ seems to be very small and these molecules may have an almost planar and rigid structure. On the other hand, the diacetylenic linkage in VI$_c$ is forced to bend owing to the length of its bridging chain, the degree of bending of the diacetylenic bond being much larger in VI_b in accordance with the shorter methylene bridge as illustrated in Fig. 1. o,o'-Dimethoxydiphenyldiacetylene ($VIII_a$) and o,o'-diethoxydiphenyldiacetylene ($VIII_b$) were prepared and the ultraviolet spectra of these open chain analogues were compared with those of VI. As indicated in Fig. 2 and Table I, the location of the absorption maxima in the spectra of VI_d and VI_e at the long wavelength region were found to be almost identical with those of the open chain models $VIII_a$ and $VIII_b$. But the absorption intensities (ε_{max}) of VI_d and VI_e are found to be larger than those of $VIII_a$ and $VIII_b$ indicating the rigid and planar structure of these cyclic diacetylenes. The sequence of decrease of the ε_{max}-values are found to be $VI_e > VI_d > VI_c > VI_b$. This sequence of the ε_{max} indicates that the planarity of the molecule increases the transition probability and the increase in the bending of diacetylenic linkage causes the decrease of the probability. It is remarkable that the λ_{max} of VI_b shifted about 12 mμ to shorter wavelength as compared with VI_d, VI_e and the open chain models. It has been already known in numerous examples, especially in substituted biphenyls[4] or substituted acetophenones[5], that relatively weak steric hindrance in the excited state of these molecules diminishes the transition probability resulting in the decrease of absorption intensity, and the presence of a strong steric hindrance in the excited state causes a hypsochromic shift of the absorption maxima as the result of the increased transition energy. As the two phenyl groups in the molecule of VI_b are held in a coplanar position owing to the short methylene bridge, the hypsochromic shift and the hyperchromic effect observed in VI_b may be attributed to the bending of the diacetylenic linkage. This may be the first example in which the bending of acetylenic linkage results in a hypsochromic shift of the characteristic K-band. The methylene chain in VI is held closely parallel with the diacetylenic unit and the ultraviolet spectra of these cycles show a sharp and intense λ_{min} at ca. 260 mμ making a sharp contrast with those of VIII and VII in which a λ_{max} exists at the same wavelength. This absorption minimum was also observed in the spectra of I (n=3 and 4). As pointed out in the previous paper[1], the disappearance of λ_{max} at this position may be ascribed to the presence of a proximity effect of the methylene group to the acetylenic linkage (Figs. 3 and 4, Table I). Also the appearance of a new λ_{max} in the spectra of VI near 230~240 mμ is the same trend as observed in I. These results are also confirmed with X_a, X_b, XIII and XV, which will be discussed in the following section.



VIIIa : $R=CH_3$ VIIIb : $R=C_2H_5$

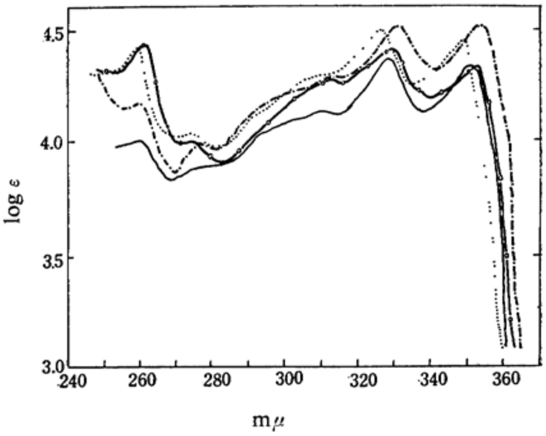


Fig. 3. The ultraviolet spectra of the cyclic dimers (VII) and $VIII_a$.
——— : VII_b in dioxane
·—·—·— : VII_d in dioxane
—○—○ : VII_e in dioxane
……… : $VIII_a$ in 95% ethanol
The curve of VII was drawn using the reduced ε values corresponding to a diyne-unit.

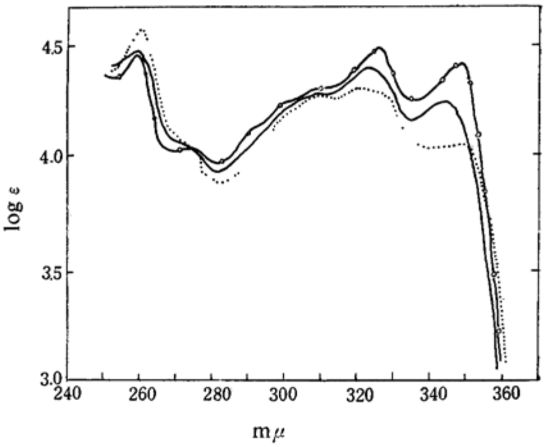


Fig. 4. The ultraviolet spectra of the cyclic dimers (VII) and $VIII_b$.
……… : VII_c in dioxane
——— : VII_a in dioxane
—○—○ : $VIII_b$ in 99.5% ethanol
The curve of VII was drawn using the reduced ε values corresponding to a diyne-unit.

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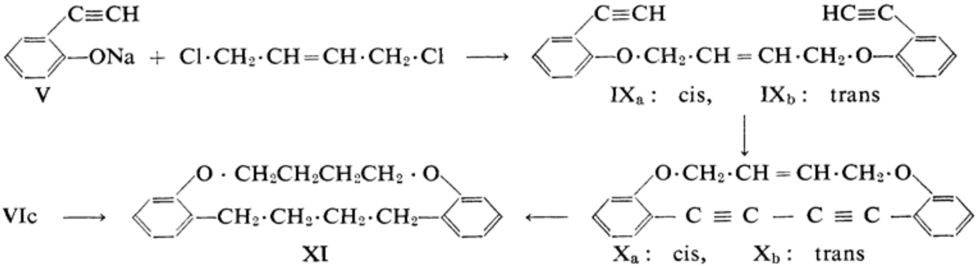
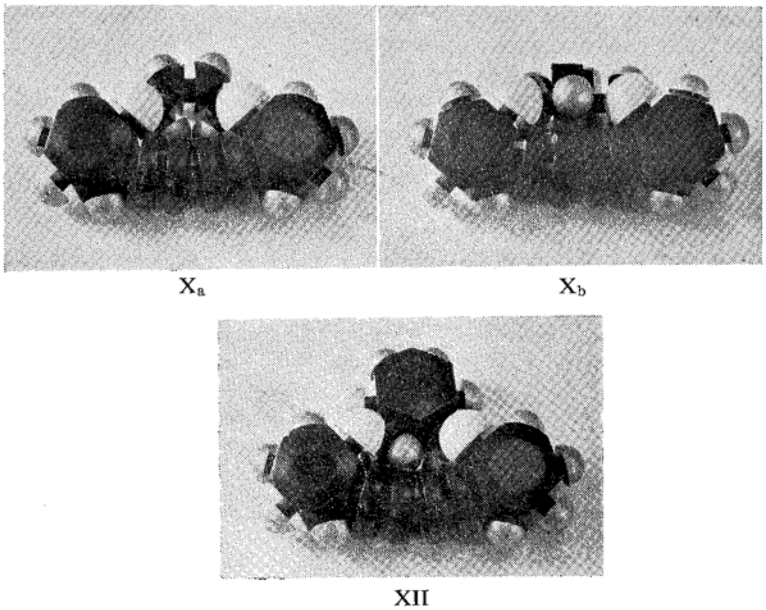
[4] E. A. Braude and E. A. Evans, *J. Chem. Soc.*, **1954**, 607; M. T. O. Shaughnessy and W. H. Rodebush, *J. Am. Chem. Soc.*, **62**, 2906 (1940).

[5] E. A. Braude, F. Sondheimer and W. F. Forbes, *Nature*, **173**, 117 (1954).

The ultraviolet spectra of VII$_b$, VII$_d$ and VII$_e$ do not depart from those of the open chain analogues as illustrated in Fig. 3 (cf. Table I). On the other hand, abnormal absorption spectra were observed in the case of VII$_a$ and VII$_c$ (Fig. 4 and Table I). An examination of the scale models of these cyclic dimers reveals that the molecule bearing a short methylene bridge of an even number of carbon atoms can not take uniplanar structure, and the abovementioned anomalous ultraviolet spectra of VII$_a$ and VII$_c$ may be attributed to the non-planar geometry of these molecules.

The reaction of sodium *o*-ethynylphenoxide (V) with *cis*- or *trans*-1, 4-dichloro-2-butene yielded the terminal diacetylene, IX$_a$ and IX$_b$, respectively. The oxidative coupling of IX by means of cupric acetate in pyridine[2)] resulted in the cyclic diacetylenes, X$_a$ and X$_b$ in a 33 and 30% yield, respectively. These diacetylenic cycles were found to be unstable to heat. It was observed that X$_a$ (m. p. 154°C (decomp.)) is completely decomposed when heated to a temperature of 145°C for 30 min. The structure of X$_a$ and X$_b$ were inferred from its analytical data and its ultraviolet and infrared spectroscopic evidences. The molecular weight of X$_a$ and X$_b$ could not be determined by Rast's method on account of its thermal instability, therefore the molecular weight of the decahydroderivatives XI were determined by Rast's method in camphor. Also the structure of XI was confirmed by the identity with the reduction product of VI$_c$. Inspection of the scale models of X$_a$ and X$_b$ indicates that the molecules involve large ring strain due to the bending of the diacetylenic linkage as shown in Fig. 5. The ultraviolet spectra of X$_a$ and X$_b$ showed a shift to shorter wavelength about 8 mμ as illustrated in Fig. 6 (Table I). This fact may be ascribed to the increase of the transition energy on account of the strong ring strain. Interestingly, enough, the ultraviolet spectrum of X$_b$ has broad absorption peaks as compared with those of X$_a$ (Fig. 6). The scale models of X$_a$ and X$_b$ indicate that the ethylenic bond in the former is held apart from the diacetylenic unit in the cycle; on the other hand, the double bond in the bridging chain in the latter molecule is held closely to




X$_a$ X$_b$

XII

Fig. 5. The molecular models of X and XII (Courtauld).

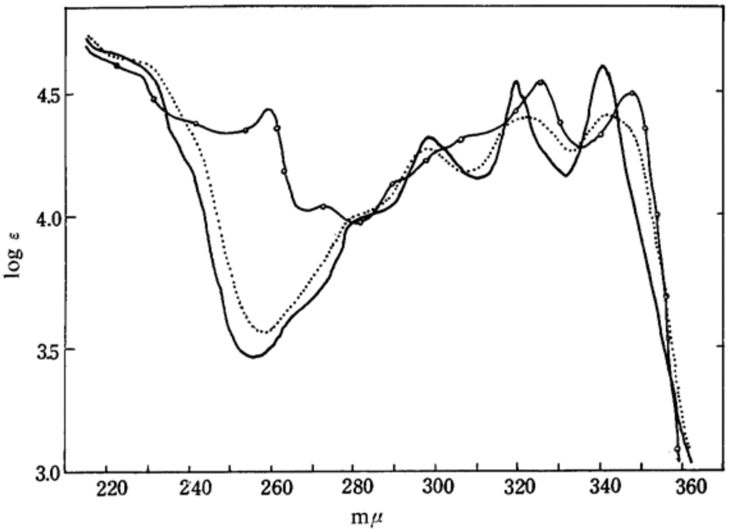


Fig. 6. The ultraviolet spectra of X and $VIII_a$ (in 99.5% ethanol).
———: X_a ········: X_b —○—○: $VIII_a$

the diacetylenic linkage (Fig. 5). Therefore the above-mentioned anomalousness of the absorption peaks of X_b seem to be associated with a transannular interaction between the π-electrons of the double bond in the bridging chain and those of the diacetylenic unit. Another example of the same type of transannular phenomenon will be discussed in the following paper[6].

The oxidative coupling of the terminal diacetylene obtained by the reaction of *o*-xylylene dibromide with V afforded the cyclic diacetylene XII and the cyclic dimer XIII in a yield of 8 and 3%, respectively. XII was found to be a heat sensitive substance, and the molecular weight was determined with the reduction product, XIV. The ultraviolet spectrum of XII does not depart from that of X_a indicating that the ring strain in XII is almost equal to that of X_a. Also the similarity of the ultraviolet spectra of XII and X_a exclude the possibility of the presence of a transannular interaction between the phenylene group in the bridging chain and the diyne unit. In the most probable geometry of the molecule of XII which was inferred from the inspection of the scale model; the *o*-phenylene group seems to hold too far apart from the diacetylenic linkage for interstitial effects to operate (Figs. 5 and 7). The fact that the cyclic dimer XIII crystallized with two moles of benzene is the same as in the case of VII_b. The configuration of XIII seem to be almost strain free, since the ultraviolet absorption spectrum of XIII is similar to those of VIII and XV as recorded in Fig. 8 and Table I.

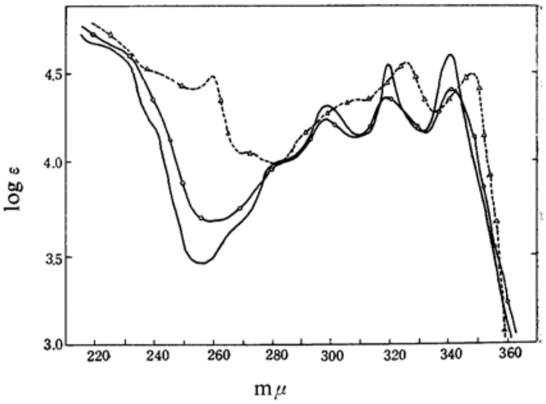
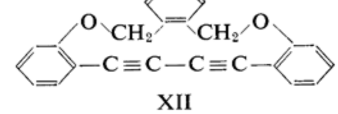
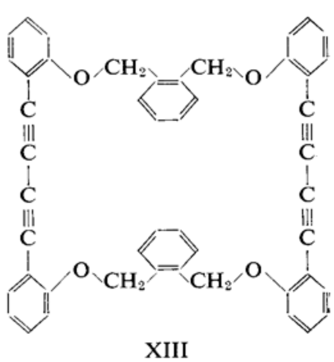


Fig. 7. The ultraviolet spectra of X_a, XII and XV (in 99.5% ethanol).
———: X_a —○—○: XII ···△···△: XV



XII



XIII

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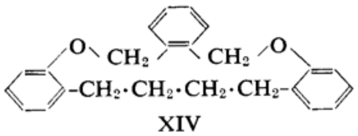
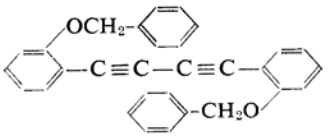
[6] F. Toda and M. Nakagawa, This Bulletin, 32, 514 (1959).


XIV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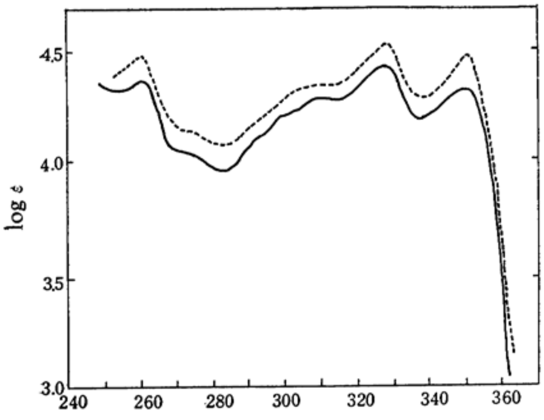


Fig. 8. The ultraviolet spectra of the cyclic tetraacetylene (XIII) and the open chain analogue (XV) (in dioxane).
——— : XIII ········· : XV
The curve of XIII was drawn using the reduced ε values corresponding to a diyne-unit.

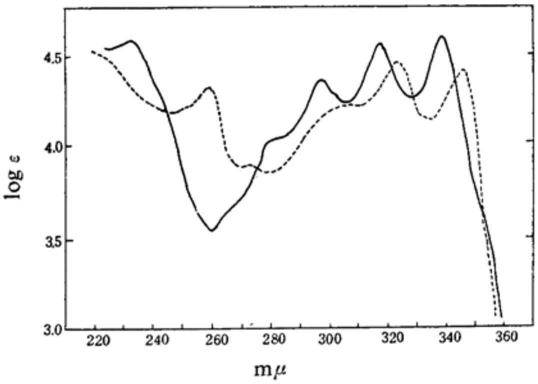
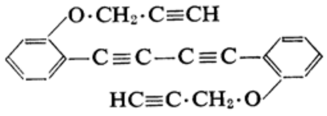
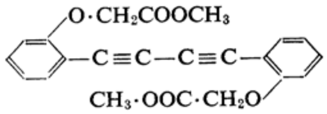
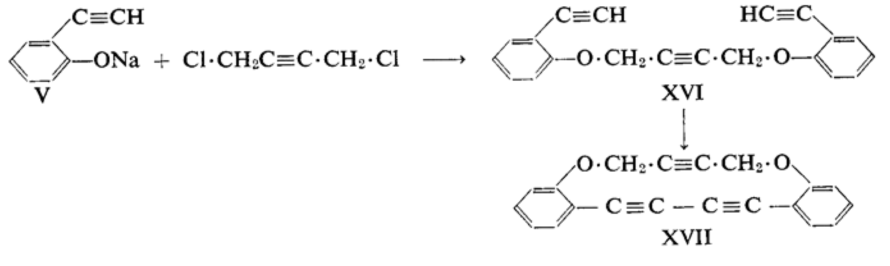


Fig. 9. The ultraviolet spectra of the cyclic triacetylene (XVII) and the open chain analogue (XVIII) (in 99.5% ethanol).
——— : XVII ------ : XVIII

The diethynyl compound XVI which was prepared by the reaction of 1,4-dichloro-2-butyne and V was oxidized according to the procedure of Eglinton. The cyclic triacetylene XVII was obtained in a yield of 3.5% as heat sensitive crystals together with a large amount of sparingly soluble amorphous solid with high melting point. The monomeric structure of XVII was inferred from the ultraviolet and infrared spectroscopic evidences. It was observed that the ultraviolet absorption maxima in the spectrum of XVII shifts to shorter wavelength (ca. 8 mμ) as compared with those of the open chain analogue (XVIII). (Fig. 9 and Table I). Substitution of a hydrogen atom in the methyl group of the phenoxy ether by an electron attracting group such as ethynyl or carboxymethyl group result in a slight hypsochromic shift of the ultraviolet spectra as illustrated in Fig. 10, therefore XVIII was chosen as a linear model of XVII. Conversly the ultraviolet spectrum of *o*,*o*′-dihydroxydiphenyldiacetylene in an aqueous alkali showed a red-shift with a change in the absorption curve as compared with that of in a neutral solution (Fig. 11). The ultraviolet spectroscopic behavior of the derivatives of *o*,*o*′-dihydroxydiphenyldiacetylene indicates that the availability of electrons on the oxygen atoms in the conjugated position to the chromophor system of *o*,*o*′-dihydroxydiphenyldiacetylene is responsible for the abovementioned blue- or red-shift of the spectrum. The heat sensitivity and the hypsochromic shift of the spectrum of XVII may be associated with the deformation of diacetylenic linkage due to the large ring strain.


XVIII


XIX



XVII

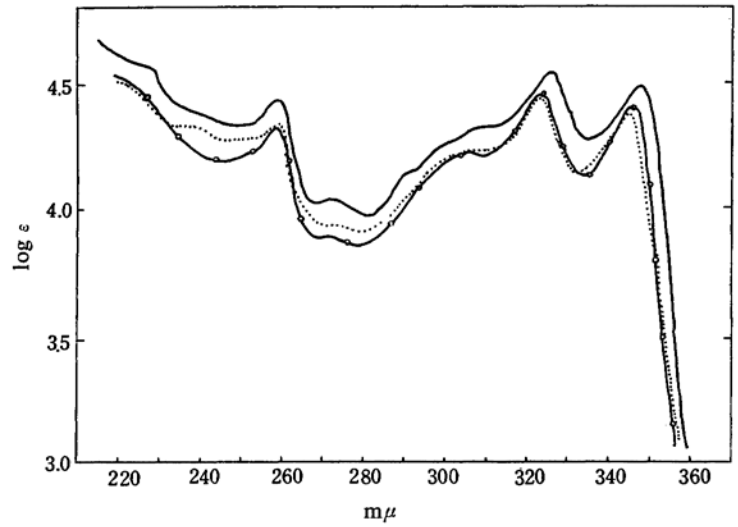


Fig. 10. The ultraviolet spectra of XVIII, XIX and VIII$_a$.

———: VIII$_a$ in 99.5% ethanol　　—○—○: XVIII in 99.5% ethanol
········: XIX in 95% ethanol

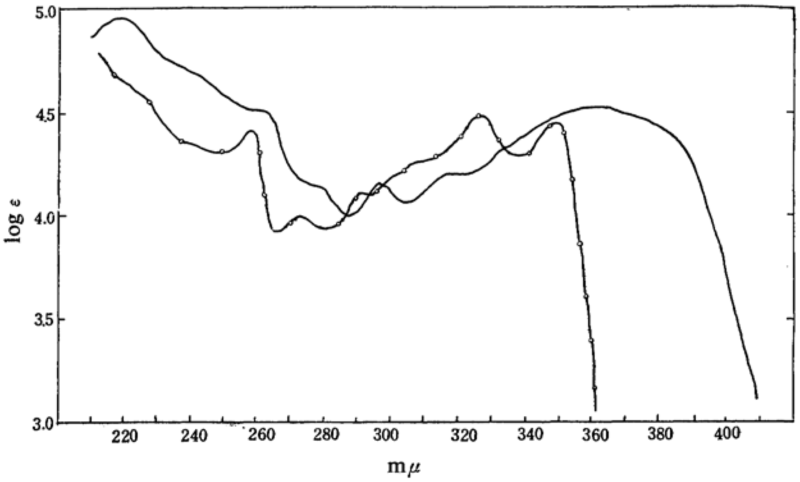


Fig. 11. The ultraviolet spectra of *o, o'*-dihydroxydiphenyldiacetylene in a neutral and an alkaline solution.

—○—○: in 99.5% ethanol　　———: in an aqueous sodium hydroxide

It was revealed from the above-mentioned observations that the bending of the diyne in the diphenyldiacetylene system in which the two phenyl groups are held in a uniplanar or in a near uniplanar position exerts a minor effect on the ultraviolet spectrum. It was well-known that the twist of single bond in a conjugate system such as *o, o'*-disubstituted acetophenones[4] or 2, 2'-disubstituted biphenyls[5] results in a remarkable change in their ultraviolet spectra. An insulation of conjugation at the position of the twisted single bond was assumed from the change of the ultraviolet spectra of *o, o'*-disubstituted acetophenones and 2, 2'-disubstituted biphenyls bearing substituents with large steric requirement. The maximal shift among the abovementioned strained cyclic diacetylenes was found to be 12 mμ. The

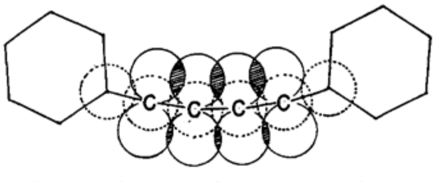


Fig. 12. A schematic illustration of p-orbital overlapping in a bent diphenyldiacetylene system.

minor effect on the bending of the diyne unit on the spectrum is quite understandable if we consider the shape of p-orbitals of conjugated acetylenic linkage. As schematically illustrated in Fig. 12, the bending of the diacetylenic linkage causes only a minor change in the overlapping of its p-orbitals. This may be the cause of the slight hypsochromic shift of the strained diacetylenic cycles.

As reported in the previous paper[1)], the smallest macrolide I, ($n=3$) was a very photosensitive substance, and the sensitivity was attributed to the bending of the diacetylenic linkage. But the highly strained ether analogues such as VI_b, X_a, X_b, XII and XVII were found to be fairly stable to light, but sensitive to heat. These findings indicate that the photosensitivity of I ($n=3$) may possibly be attributable to a photochemical reaction of the carbonyl function with the acetylenic bond which is held in the proximity of the ester linkage or the creavage of the strained ester linkage by the photoexcitation on the molecule. To confirm this point, it appeared desirable to examine the photosensitivity of another cyclic diacetylene containing carbonyl function in the bridging chain. The present authors have attempted the synthesis of a keto-ether derivative of *o, o'*-dihydroxydiphenyldiacetylene. The high dilution Dieckmann condensation of carbomethoxymethyl ether of *o,o'*-dihydroxydiphenyldiacetylene (XIX)[1)] to yield a cyclic ketocarboxylate resulted in the formation of a brown red resinous material, and the expected ketoester could not be isolated.

Experimental**

1, 5-Bis-(*o*-acetylphenoxy)-pentane (III, $n=5$).— *o*-Hydroxyacetophenone (10.9 g., 0.08 mol.) was added to an ethanolic solution of sodium ethoxide (sodium, 2.0 g. and absolute ethanol, 25 ml.), and the solvent was removed under reduced pressure. The sodium phenoxide thus obtained II was mixed with 1,5-diiodopentane (13.6 g., 0.042 mol.) and the mixture was heated to 160~170°C for 4 hr. The cooled reaction mixture was filtered and the solid was washed with ethanol, hot water and ethanol, successively. The dried material was recrystallized from benzene or ethanol yielding III ($n=5$), colorless needles, m. p. 104~105°C. 5.5 g. (40%).

Found: C, 74.14; H, 7.16. Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11%.

IR max., 1665 (C=O), 1245 (=C-O-) cm⁻¹.

1, 6-Bis-(*o*-acetylphenoxy)-hexane (III, $n=6$).— The reaction of 1,6-diiodohexane and II according to the method similar to that described above resulted in III ($n=6$), colorless plates or needles, m. p. 121°C in a yield of 42%.

Found: C, 74.80; H, 7.47. Calcd. for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39%.

IR max., 1667 (C=O), 1250 (=C-O-) cm^{-1}.

1, 4-Bis-(*o*-acetylphenoxy)-butane (III, $n=4$).— The reaction of II with 1,4-diiodobutane was carried out according to the above-mentioned procedure yielding III ($n=4$), colorless needles, m. p. 147°C in a yield of 34%.

Found: C, 73.18; H, 6.88. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79%.

IR max., 1665 (C=O), 1242, 1231 (=C-O-) cm^{-1}.

Syntheses of IV ($n=4$, 5 and 6) from III. — The mixture of phosphorus pentachloride (12.0 g., 0.058 mol.), $III_{n=6}$ (9.0 g., 0.025 mol.) and phosphorus oxychloride (15 ml.) was heated to 80~85°C for 45 min. The phosphorus oxychloride was removed under reduced pressure. The crude chloride thus obtained was dissolved in anhydrous ether (50 ml.). The ethereal solution was added into the solution of sodamide in liquid ammonia (prepared from sodium, 5 g., 0.23 mol. and ammonia, 200 ml.) during a period of 20 min. under mechanical stirring. Stirring was continued for a further 1.5 hr., and the ammonia was allowed to evaporate. The residual solid was mixed with water (200 ml.) and extracted with ether (350 ml.). The extract was washed with water and dried over magnesium sulfate. The solvent was distilled, resulting in a crystalline solid. The solid was recrystallized repeatedly from ethanol using active charcoal to yield $IV_{n=6}$, colorless needles, m. p. 89~90°C, 3.8 g. (47%).

Found: C, 82.49; H, 7.22. Calcd. for $C_{22}H_{22}O_2$: C, 82.98; H, 6.96%.

IR max., 3270 (-C≡CH), 1245 (=C-O-) cm^{-1}.

The reaction of $III_{n=5}$ with phosphorus pentachloride followed by dehydrochlorination yielded $IV_{n=5}$, colorless needles, m. p. 91.5~92°C, (38%).

Found: C, 82.65; H, 6.85. Calcd. for $C_{21}H_{20}O_2$: C, 82.86; H, 6.62%.

IR max., 3280 (-C≡CH), 2110 (-C≡C-), 1252 (=C-O-) cm^{-1}.

Similar treatment of $III_{n=4}$ afforded $IV_{n=4}$, colorless prisms, m. p. 82°C, (40%).

Found: C, 82.43; H, 6.24. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25%.

IR max., 3250 (-C≡C-), 1250 (=C-O-) cm^{-1}.

Syntheses of IV ($n=1$, 2, 3 and 4) from V. — *o*-Hydroxyphenylacetylene (2.3 g., 0.02 mol.) was added to a solution of sodium ethoxide in ethanol (sodium, 0.5 g. and absolute ethanol, 5 ml.). The solvent was removed under reduced pressure at room temperature to yield V. A solution of 1,4-diiodobutane (3.1 g., 0.01 mol.) in dimethylformamide (20 ml.) was added to V, and the mixture was refluxed for 2.5 hr. The cooled reaction mixture was poured into ice-water (200 ml.). The crude crystals deposited were filtered, then washed with water and ethanol, successively. The crude $IV_{n=4}$ thus obtained was recrystallized from ethanol using active charcoal to give pure $IV_{n=4}$, colorless prisms, m. p. 82°C, 1.7 g. (59%), undepressed on admixture with $IV_{n=4}$ which was derived from $III_{n=4}$.

The reaction of *o*-hydroxyphenylacetylene (1.5 g.)

** No melting points were corrected. Infrared spectra were measured by the Nujol mull method and molecular weights were obtained by the Rast method (in camphor). Otherwise some special indication was given.

with 1,3-dibromopropane according to the abovementioned procedure yielded crude $IV_{n=3}$ as a viscous oil, (1.7 g.), IR max., 3400 (-C≡CH), 2160 (-C≡C-), 1260 (=C-O-) cm^{-1}. The crude oil was used without further purification for the oxidative coupling.

A similar reaction of *o*-hydroxyphenylacetylene (1.5 g.) with ethylene dibromide gave $IV_{n=2}$, colorless prisms, m. p. 150°C, 250 mg., (15%).

Found: C, 82.27; H, 5.29. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38%.

IR max., 3280 (-C≡CH), 2130 (-C≡C-), 1252 (=C-O-) cm^{-1}.

Similarly the reaction of *o*-hydroxyphenylacetylene (1.5 g.) with dibromomethane yielded $IV_{n=1}$, viscous oil, (1.9 g.), IR max., 3370 (-C≡CH), 2160 (-C≡C-) and 1230 (=C-O-) cm^{-1}.

Oxidative Coupling of $IV_{n=6}$. —The mixture of cupric acetate monohydrate (15 g.), pyridine (150 g.) and $IV_{n=6}$ (1.5 g.) was stirred for 4 hr. at 55~60°C. The solvent was distilled under reduced pressure at a temperature below 40°C. Water was added to the residue, and extracted with ether (300 ml.). The extract was washed with an aqueous solution of cupric acetate and water, successively. The ether solution was dried over anhydrous magnesium sulfate. The residue obtained by evaporating the solvent was dissolved in benzene (20 ml.) and treated with active charcoal. The crude crystals obtained by concentrating benzene were fractionally recrystallized from ethyl acetate. The crystals from the more soluble portions were recrystallized from aqueous acetic acid to yield pure VI_e, colorless needles, m. p. 130°C, 0.6 g. (40%).

Found: C, 83.43; H, 6.59. Mol. wt., 322. Calcd. for $C_{22}H_{20}O_2$: C, 83.51; H, 6.37%. Mol. wt., 316.

IR max., 2150 (-C≡C-), 1272, 1243 (=C-O-) cm^{-1}.

The crystals obtained from the less soluble portions were recrystallized from ethyl acetate yielding VII_e, colorless needles, m. p. 207~208°C, 0.15 g. (10%). The melting point of this substance changed to 184~185°C on standing at room temperature for several days.

Found: C, 83.13; H, 6.49. Mol. wt., 630. Calcd. for $C_{44}H_{40}O_4$: C, 83.51; H, 6.37%. Mol. wt., 632.

IR max., 2137 (-C≡C-), 1250 (=C-O-) cm^{-1}.

Oxidative Coupling of $IV_{n=5}$.—$IV_{n=5}$ (1.0 g.) was added to the mixture of pyridine (150 g.) and cupric acetate monohydrate (10 g.), and the mixture was stirred for 3 hr. at 55°C. The crude crystals obtained by the treatment of the reaction mixture were recrystallized repeatedly from aqueous acetone yielding needles mixed with a small amount of crystalline grains. The crystalline mixture was digested with ethyl acetate to dissolve the needles. The insoluble crystalline grains were filtered and the filtrate was concentrated to dryness. Repeated recrystallization of the residual solid from aqueous acetone yielded pure VI_d, colorless needles, m. p. 132~132.5°C, 0.4 g. (40%).

Found: C, 83.27; H, 5.93. Mol. wt., 312. Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00%. Mol. wt., 302.

IR max., 2200 (-C≡C-), 1250 (=C-O-) cm^{-1}.

The elementary analysis of the crystalline grains (m. p. 180~181°C) could not be performed owing to its small amount, but the molecular weight determination (Found: 514) indicates that the grains should be the cyclic dimer (VII_d, $C_{42}H_{36}O_4$: Mol. wt., 604) of $IV_{n=5}$. IR max., 2200, 2137 (-C≡C-), 1250 (=C-O-) cm^{-1}.

Oxidative Coupling of $IV_{n=4}$. —A solution of $IV_{n=4}$ (1.0 g.) and cupric acetate monohydrate (10.0 g.) in pyridine (100 g.) was stirred for 4 hr. at 50°C. The crude crystals isolated from the reaction mixture were digested with hot ethanol. The insoluble material was filtered, and the filtrate was cooled to deposite crystals. The crystals, on recrystallization from ethanol, gave pure VI_c, colorless needles or plates, m. p. 96 or 112°C, 0.4 g. (40%). It was observed that VI_c melts at 112°C when the temperature of a heating bath is gradually raised from room temperature. But VI_c melts at 96°C when the bath was heated previously to 80°C. The solid obtained by cooling the molten crystals melts at 112°C by the ordinary method of measurement, but it melts also at 96°C in a preheated bath.

Found: C, 83.01; H, 5.42. Mol. wt., 271. Calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59%. Mol. wt., 288.

IR max., 2210 (-C≡C-), 1240 (=C-O-) cm^{-1}.

The above-mentioned insoluble solid was recrystallized from ethyl acetate yielding VII_c, colorless needles, m. p. 237~238°C, 20 mg. (2%).

Found: C, 82.52; H, 5.45. Mol. wt., 533. Calcd. for $C_{40}H_{32}O_4$: C, 83.31; H, 5.59%. Mol. wt., 576.

IR max., 2210, 2150 (-C≡C-), 1240 (=C-O-) cm^{-1}.

Hydrogenation of VI_c.—VI_c (100 mg.) in benzene (15 ml.) was reduced over 5% palladium-on-charcoal (20 mg.). After removal of the solvent in a vacuum, the residue was recrystallized from aqueous ethanol yielding XI, colorless plates, m. p. 63.5°C, 100 mg.

Found: C, 80.48; H, 8.09. Mol. wt., 303. Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16%. Mol. wt., 296.

XI showed no depression of the mixed melting point on admixture with the hydrogenation products of X_a and X_b. Also the infrared spectra of these saturated macrocycles are found to be identical over the entire region of wavelength.

Oxidative Coupling of $IV_{n=3}$. —Treatment of $IV_{n=3}$ (1.7 g.) with Eglinton's reagent (cupric acetate monohydrate, 10 g. and pyridine, 100 g.) at 47°C for 4 hr. gave crude crystals. The crude material was digested with hot ethanol (30 ml.) to remove the insoluble material. The crystals obtained by diluting the ethanolic solution with water was recrystallized repeatedly from aqueous ethanol to give pure VI_b, colorless needles, m. p. 115°C, (decomp.), 50 mg. (3%).

Found: C, 83.31; H, 5.34. Calcd. for $C_{19}H_{14}O_2$: C, 83.20; H, 5.15%.

IR max., 2210 (-C≡C-), 1227 (=C-O-) cm^{-1}.

The monomeric nature of VI_b was deduced from the X-ray crystallographic data (space group, C^6_{2h}—C^2/c, dimension of unit cell, a=22.22 Å, b=13.04 Å, c=11.20 Å, Z=8).

The abovementioned ethanol insoluble material was dissolved in benzene and treated with active charcoal. The crystals deposited from the benzene solution were recrystallized from benzene resulting in VII_b, colorless needles, m. p. 228~229°C (decomp.), 20 mg. (1%). It was observed that the transparent crystals on the hot stage of a Kofler block became turbid at about 100°C. This phenomenon could be ascribed to the loss of the solvent of crystallization (benzene).

Found: C, 85.13; H, 5.76, benzene of crystallization, 22.47%. Calcd. for $C_{38}H_{28}O_4 \cdot 2C_6H_6$: C, 85.20; H, 5.72, benzene of crystallization, 22.03%.

The analytical data of the solvent-free material was found to be as follows:

Found: C, 83.83; H, 5.11. Mol. wt., 534. Calcd. for $C_{38}H_{28}O_4$: C, 83.20; H, 5.15%. Mol. wt., 548.

IR max., 2160 (-C≡C-), 1250 (=C-O-) cm^{-1}.

Oxidative Coupling of $IV_{n=2}$. — A mixture of $IV_{n=2}$ (200 mg.), cupric acetate monohydrate (3.0 g.) and pyridine (30 g.) was kept for 4.5 hr. at 40°C under mechanical stirring. The reaction mixture was treated according to the usual manner. The crude crystals thus obtained were recrystallized from ethyl acetate or ethyl acetate-methanol yielding VII_a, colorless needles, m. p. 250~252°C (decomp.), 5 mg. (2.5%), Mol. wt., 505. Calcd. for $C_{36}H_{24}O_4$: Mol. wt., 520. IR max., 1245 (=C-O-) cm^{-1}.

***o, o'*-Dimethoxydiphenyldiacetylene ($VIII_a$).**—*o*, *o'*-Dihydroxydiphenyldiacetylene (1.0 g., 0.043 mol.) was dissolved in an ethanolic solution of sodium ethoxide (sodium, 0.23 g. and absolute ethanol, 30 ml.). Methyl iodide (14.2 g., 0.1 mol.) was added to the solution. The mixture changed to neutral after heating at 50~60°C for 0.5 hr. and at 95°C for 1 hr. The crystals obtained by cooling the reaction mixture were filtered, then washed with water and ethanol, successively. The crude material was recrystallized from ethanol giving $VIII_a$, colorless prisms, m. p. 138°C, 1.0 g. (90%).

Found: C, 82.13; H, 5.57. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38%.

IR max., 2146 (-C≡C-), 1246 (=C-O-) cm^{-1}. (measured by KBr-disk method).

***o, o'*-Diethoxydiphenyldiacetylene ($VIII_b$).** — A mixture of *o,o'*-dihydroxydiphenyldiacetylene (1.0 g., 0.0043 mol.), sodium ethoxide in ethanol (sodium, 0.46 g. and absolute ethanol, 20 ml.) and ethyl bromide (10 g., 0.1 mol.) was heated to 55~60°C for 30 min. and to 95°C for 2 hr. The neutral reaction mixture was filtered to remove the inorganic salt. Water was added to the filtrate and extracted with ether (50 ml.). The extract was washed with aqueous potassium hydroxide and water, successively, and dried over anhydrous magnesium sulfate. The oily material obtained by evaporating the solvent changed gradually to a crystalline mass. $VIII_a$ was obtained as colorless needles, m. p. 72°C, 1.1 g. (91%) on the recrystallization of the mass from ethanol.

Found: C, 82.59; H, 6.27. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25%.

IR max., 2180 (-C≡C-), 1250 (=C-O-) cm^{-1}.

Synthesis of IX_b.—*o*-Hydroxyphenylacetylene (2.1 g., 0.018 mol.) was dissolved in a solution of sodium ethoxide in ethanol (sodium, 0.4 g. and absolute ethanol, 5 ml.). After removal of the alcohol in a vacuum at room temperature, the residue was mixed with *trans*-1,4-dichloro-2-butene (1.2 g., 0.009 mol.), a catalytic amount of potassium iodide and dimethylformamide (20 ml.) and the mixture was refluxed for 1 hr. The neutral reaction mixture was poured into ice-water. The crystals deposited were filtered, then washed with water and ethanol, successively. The crude crystals were recrystallized from ethanol yielding IX_b, colorless leaflets, m. p. 118~119°C, 1.5 g. (60%).

Found: C, 82.72; H, 5.66. Calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59%.

IR max., 3255 (-C≡CH), 2105 (-C≡C-), 1240 (=C-O-), 975 (*trans*-ethylene) cm^{-1}.

Synthesis of IX_a. — The reaction of *cis*-1,4-dichloro-2-butene (1.2 g., 0.009 mol.) with *o*-hydroxyphenylacetylene (2.1 g., 0.018 mol.) according to the same procedure as that described above yielded IX_a, red oil, 2.3 g. (85%).

IR max., 3400 (-C≡CH), 2160 (-C≡C-), 1250 (=C-O-) cm^{-1}.

The crude IX_a was employed without further purification to the subsequent reaction.

Oxidative Coupling of IX_a. — IX_a (2.3 g.) was oxidized with cupric acetate monohydrate (15 g.) in pyridine (110 g.). After stirring for 4 hr. at 50~52°C, the solvent was removed under reduced pressure at a temperature below 30°C. The residue was extracted with ether (250 ml.), washed with aqueous cupric acetate and water, successively, and dried over anhydrous sodium sulfate. The crude crystals from the ether extract, on repeated recrystallization from benzene, gave X_a, colorless prisms, m. p. 154°C (decomp.), 0.7 g. (33%). Complete decomposition was observed when the crystals were heated to 140°C for 30 min.

Found: C, 83.73; H, 4.94. Calcd. for $C_{20}H_{14}O_2$: C, 83.90; H, 4.93%.

IR max., 2230, 2165 (-C≡C-), 1257, 1215 (=C-O-), 742, 720 (*cis*-ethylene) cm^{-1}.

The monomeric nature of X_a was inferred from the molecular weight of the reduction product XI.

Hydrogenation of X_a.—X_a (200 mg.) in benzene (20 ml.) was hydrogenated over 5% palladium-on-charcoal (20 mg.). The reduction product was recrystallized from aqueous ethanol yielding XI, colorless plates, m. p. 63.5°C, 200 mg. (96%). This substance showed no depression of the melting point on admixture with the reduction product of VI_c and X_b. Also the infrared spectra of these reduction products were found to be identical over the entire region of wavelength.

Oxidative Coupling of IX_b.—A solution of IX_b (1.3 g.) and cupric acetate monohydrate (15 g.) in pyridine (120 g.) was heated to 50°C for 3 hr. Treatment of the reaction mixture according to the usual method afforded crude crystals. The crude material was repeatedly recrystallized from ethyl acetate containing a small amount of ethanol yielding X_b, colorless plates, m. p. 130°C (decomp.), 0.4 g. (30%).

Found: C, 83.80; H, 5.02. Calcd. for $C_{20}H_{14}O_2$: C, 83.90; H, 4.93%.

IR max., 2205 (-C≡C-), 1237 (=C-O-), 960 (*trans*-ethylene) cm^{-1}.

Hydrogenation of X_b.—Hydrogenation of X_b in benzene over 5% palladium-on-charcoal gave XI, colorless plates, m. p. 63.5°C in a yield of 96%.

Syntheses of XII and XIII. — *o*-Hydroxyphenylacetylene (2.4 g., 0.02 mol.) was dissolved in a solution of sodium methoxide in methanol (sodium, 0.5 g. and absolute methanol, 7 ml.). After removal of the solvent under reduced pressure at room temperature, the residue was mixed with *o*-xylylene dibromide (2.7 g., 0.01 mol.), a trace of potassium iodide and dimethylformamide (20 ml.), and the mixture was refluxed for 1.5 hr. The cooled neutral reaction mixture was poured into ice-water, and extracted with ether. The ether layer was washed with water and dried over magnesium sulfate. The viscous oil (3.5 g., IR max., 3360 (-C≡CH), 2160 (-C≡C-), 1250 (=C-O) cm^{-1}) from the ether layer, was mixed with a solution of cupric acetate monohydrate (15 g.) in pyridine (150 g.). The mixture was stirred for 4 hr. at 50°C. Isolation with ether as before yielded crude crystals. The crude substance was washed with a small amount of cold benzene and digested with hot ethanol. The insoluble material was removed by filtration. The crystals from the filtrate were recrystallized from ethanol to yield XII, colorless needles, m. p. 148.5°C, (decomp.), 250 mg. (8%).

Found: C, 85.37; H, 4.83. Calcd. for $C_{24}H_{16}O_2$: C, 85.69; H, 4.79%.

IR max., 2220 (-C≡C-), 1222, 1208 (=C-O-), 1375 (δ CH) cm^{-1}. (measured by KBr-disk method).

It is to be noted that the infrared spectrum of XII lacks the absorption peak arising from the stretching of methyl group.

Owing to the thermal instability, the molecular weight of XII was inferred from that of the reduction product XIV.

The abovementioned insoluble solid was recrystallized from benzene yielding XIII, colorless plates, m. p. 230∼231°C, 100 mg. (3%). It was observed that the transparent crystals turn to opaque at about 100°C. This phenomenon is attributable to the loss of benzene of crystallization. The amount of benzene of crystallization was found to be 19.06%. (Calcd. for $C_{48}H_{32}O_4 \cdot 2C_6H_6$: 18.84%).

Found: C, 85.29; H, 4.82. Mol. wt., 667. Calcd. for $C_{48}H_{32}O_4$: C, 85.69; H, 4.79%. Mol. wt., 672.

IR max., 1240 (=C-O-) cm^{-1}.

Hydrogenation of XII.—XII (130 mg.) in benzene (15 ml.) was reduced over 5% palladium-on-charcoal (20 mg.). After removal of the catalyst, the solvent was distilled and the residual solid was recrystallized from ethyl acetate-ethanol resulting in XIV, colorless needles, m. p. 180°C, 125 mg.

Found: C, 83.55; H, 7.06. Mol. wt., 346. Calcd. for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02, Mol. wt., 344.

IR max., 2930, 2865 (ν CH), 1383 (δ CH), 1230 (=C-O-) cm^{-1} (KBr-disk).

***o,o*′-Dibenzyloxydiphenyldiacetylene** (XV).—*o,o*′-Dihydroxydiphenyldiacetylene (1.0 g., 0.0086 mol.) and a trace of potassium iodide were added to a solution of sodium ethoxide in ethanol (sodium, 0.2 g., and absolute ethanol, 20 ml.). After refluxing for 1 hr., the reaction mixture was cooled. The crystals deposited were filtered, then washed with water and ethanol, successively. The crude material was recrystallized from benzene or ethyl acetate to give XV, colorless needles, m. p. 152∼152.5°C, 0.9 g. (53%).

Found: C, 86.91; H, 5.23. Calcd. for $C_{30}H_{22}O_2$: C, 86.93; H, 5.35%.

Synthesis of XVI. — *o*-Hydroxyphenylacetylene (1.5 g., 0.013 mol.) was dissolved in a solution of sodium ethoxide in ethanol (sodium, 0.3 g. and absolute ethanol, 5 ml.). After the removal of the ethanol at room temperature in a vacuum, the residue was mixed with 1,4-dichloro-2-butyne (0.8 g., 0.0065 mol.), dimethylformamide (13 ml.) and a catalytic amount of potassium iodide, and refluxed for 1.5 hr. The cooled reaction mixture was poured into ice-water and extracted with ether (100 ml.). The extract was washed with aqueous potassium hydroxide and water, successively, and dried over sodium sulfate. The crude crystals obtained by evaporating the ethereal solution were purified by repeated recrystallization from aqueous ethanol resulting in XVI, colorless needles, m. p. 75°C, 0.5 g. (35%).

Found: C, 83.48; H, 5.01. Calcd. for $C_{20}H_{14}O_2$: C, 83.90; H, 4.93%.

IR max., 3370 (-C≡CH), 1240 (=C-O-) cm^{-1}.

Oxidative Coupling of XVI. — The mixture of XVI (420 mg.), cupric acetate monohydrate (4.5 g.) and pyridine (45 g.) was stirred at 40°C for 4 hr. and then at 50°C for 1 hr. The solvent was removed under reduced pressure at a temperature below 35°C. The residue thus obtained was extracted with ether (100 ml.). An amorphous solid with high melting point suspended in ethereal solution was removed by filtration (300 mg.). No investigation on the nature of the amorphous solid was carried out. The ethereal solution was treated according to the usual procedure yielding crude XVI. This was recrystallized from benzene-light petroleum (b. p. 60∼70°C) to give pure XVI, colorless needles, m. p. 167°C (decomp.), 15 mg. (3.5%).

Found: C, 84.48; H, 4.06. Calcd. for $C_{20}H_{12}O_2$: C, 84.49; H, 4.25%.

IR max., 2230 (-C≡C-), 1267 (=C-O-) cm^{-1}.

XVI was found to be a heat sensitive substance. The crystals of XVI changed to pink, then to red when heated to 120°C and melted at 167°C, forming a reddish brown liquid.

Synthesis of XVIII. — *o,o*′-Dihydroxydiphenyldiacetylene (1.1 g., 0.047 mol.) was dissolved in a solution of sodium ethoxide in ethanol (sodium, 0.2 g. and absolute ethanol, 20 ml.). Propargyl bromide (1.1 g., 0.094 mol.) and a small amount of potassium iodide were added to the ethanolic solution and refluxed for 1.5 hr. The crude crystals obtained by chilling the reaction mixture were washed with ethanol, hot water and ethanol, successively. The crude substance thus obtained was recrystallized from benzene-light petroleum (b. p. 60∼70°C). It was observed that the crystals were contaminated with a small amount of 2,2′-dibenzofuranyl6). The last mentioned substance was removed by digesting the crude crystals with benzene. The crystals remained were recrystallized from benzene resulting in XVIII, colorless needles, m. p. 151∼152°C (decomp.), 200 mg., (14%).

Found: C, 84.89: H, 4.64. Calcd. for $C_{22}H_{14}O_2$: C, 85.14; H, 4.55%.

IR max., 3270 (-C≡CH), 2160, 2130 (-C≡C-), 1225 (=C-O-) cm^{-1}.

The attempt of the intramolecular oxidative coupling of XVIII resulted in the formation of a resinous material.

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Department of Chemistry
Faculty of Science
Osaka University
Nakanoshima, Osaka